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| Substitute for form 1449/PTO<br><br><b>INFORMATION DISCLOSURE<br/>STATEMENT BY APPLICANT</b><br><i>(Use as many sheets as necessary)</i> |   |    |    | <b>Complete if Known</b> |                     |
|  |   |    |    | Application Number       | 09/900,364          |
|  |   |    |    | Filing Date              | July 5, 2001        |
|  |   |    |    | First Named Inventor     | Paul D. van Poelje  |
|  |   |    |    | Art Unit                 | 1617                |
|  |   |    |    | Examiner Name            | Leonard M. Williams |
| Sheet  | 1 | of | 10 | Attorney Docket Number   | MET-037CXT          |

| U.S. PATENT DOCUMENTS |                       |  |                                |  |   |
|-----------------------|-----------------------|--|--------------------------------|--|---|
| Examiner Initials*    | Cite No. <sup>1</sup> | Document Number                          | Publication Date<br>MM-DD-YYYY | Name of Patentee or<br>Applicant of Cited Document | Pages, Columns, Lines,<br>Where Relevant Passages<br>or Relevant Figures Appear |
|                       |                       | Number-Kind Code <sup>2</sup> (If Known) |                                |  |   |
|                       | 1.                    | 3,551,422                                | 12-29-1970                     | Tesoro, et al.                                     | All   |
|                       | 2.                    | 3,650,670                                | 03-01-1972                     | Tesoro, et al.                                     | All   |
|                       | 3.                    | 3,657,282                                | 04-18-1972                     | Christensen, et al.                                | All   |
|                       | 4.                    | 3,822,296                                | 07-02-1974                     | Christensen, et al.                                | All   |
|                       | 5.                    | 3,931,206                                | 01-06-1976                     | Bowler, et al.                                     | All   |
|                       | 6.                    | 4,000,305                                | 12-26-1976                     | Bowler, et al.                                     | All   |
|                       | 7.                    | 4,046,841                                | 09-06-1977                     | Foster, et al.                                     | All   |
|                       | 8.                    | 4,092,323                                | 05-30-1978                     | Foster, et al.                                     | All   |
|                       | 9.                    | 4,587,256                                | 05-06-1986                     | Hasler, et al.                                     | All   |
|                       | 10.                   | 4,746,654                                | 05-24-1988                     | Breliere, et al.                                   | All   |
|                       | 11.                   | 4,728,739                                | 03-01-1988                     | Kees, et al.                                       | All   |
|                       | 12.                   | 4,791,125                                | 12-13-1988                     | Clark, D.  | All   |
|                       | 13.                   | 4,876,248                                | 10-24-1989                     | Breliere, et al.                                   | All   |
|                       | 14.                   | 4,939,130                                | 07-01-1990                     | Jaeggi, et al.                                     | All   |
|                       | 15.                   | 5,116,919                                | 05-01-1992                     | Buzinkai, et al.                                   | All   |
|                       | 16.                   | 5,133,972                                | 07-28-1992                     | Ferrini et al.                                     | All   |
|                       | 17.                   | 5,142,000                                | 08-01-1992                     | Wheland, et al.                                    | All   |
|                       | 18.                   | 5,236,941                                | 08-17-1993                     | Zask, et al.                                       | All   |
|                       | 19.                   | 5,457,109                                | 10-10-1995                     | Antonucci, et al.                                  | All   |
|                       | 20.                   | 5,468,762                                | 11-21-1995                     | Malamas, et al.                                    | All   |
|                       | 21.                   | 5,478,853                                | 12-26-1995                     | Regnier, et al.                                    | All   |
|                       | 22.                   | 5,532,256                                | 07-02-1996                     | Malamas, et al.                                    | All   |
|                       | 23.                   | 5,550,276                                | 08-27-1996                     | Wirth, et al.                                      | All   |
|                       | 24.                   | 5,610,210                                | 03-11-1997                     | Holderbaum, et al.                                 | All   |
|                       | 25.                   | 5,728,650                                | 03-01-1998                     | Fisher, et al.                                     | All   |
|                       | 26.                   | 5,731,299                                | 03-01-1998                     | Ebetino, et al.                                    | All   |
|                       | 27.                   | 5,798,340                                | 08-25-1998                     | Bischofberger, et al.                              | All   |
|                       | 28.                   | 5,925,656                                | 07-20-1999                     | Kallam, et al.                                     | All   |
|                       | 29.                   | 5,958,904                                | 09-28-1999                     | Cordi, et al.                                      | All   |
|                       | 30.                   | 5,985,858                                | 11-16-1999                     | Miyata et al.                                      | All   |
|                       | 31.                   | 6,001,862                                | 12-14-1999                     | Maeda, et al.                                      | All   |
|                       | 32.                   | 6,028,052                                | 02-22-2000                     | Heyman, et al.                                     | All   |
|                       | 33.                   | 6,110,903                                | 08-29-2000                     | Kasibhatla, et al.                                 | All   |
|                       | 34.                   | 6,200,998                                | 03-13-2001                     | Sahoo, et al.                                      | All   |
|                       | 35.                   | 6,284,672                                | 09-01-2001                     | Yu, et al.   | All   |
|                       | 36.                   | 6,008,237                                | 12-01-1999                     | Sahoo, et al.                                      | All   |
|                       | 37.                   | 6,030,990                                | 02-29-2000                     | Maeda, et al.                                      | All   |

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| Examiner Signature | Date Considered |
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|  |   |    |    | Examiner Name            | Leonard M. Williams |
| Sheet  | 2 | of | 10 | Attorney Docket Number   | MET-037CXT          |

|  |     |              |            |                    |     |
|--|-----|--------------|------------|--------------------|-----|
|  | 38. | 6,037,335 B1 | 03-14-2000 | Takashima, et al.  | All |
|  | 39. | 6,054,587    | 04-01-2000 | Reddy, et al.      | All |
|  | 40. | 6,284,748 B1 | 08-01-2001 | Dang, et al.       | All |
|  | 41. | 6,294,672 B1 | 09-01-2001 | Reddy, et al.      | All |
|  | 42. | 2003/0073728 | 04-17-2003 | Van Poelje, et al. | All |

| FOREIGN PATENT DOCUMENTS |                       |   |                                |   |  |                |
|--------------------------|-----------------------|---|--------------------------------|---|--|----------------|
| Examiner Initials*       | Cite No. <sup>1</sup> | Foreign Patent Document   | Publication Date<br>MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant<br>Passages or Relevant Figures Appear | T <sup>6</sup> |
|                          |                       | Country Code <sup>2</sup> Number <sup>3</sup> Kind Code <sup>5</sup> (if known) |                                |   |  |                |
|                          | 43.                   | AU 654899B B2   | 09-09-1993                     | De Nanteuil, et al.                             | All  |                |
|                          | 44.                   | DE 195 01 843 A1  | 6-20-1996                      | Vass, et al.                                    | All  |                |
|                          | 45.                   | DE 40 29 444 A1   | 03-28-1991                     | Maier, et al.                                   | All  |                |
|                          | 46.                   | EP 0 033 195 A1   | 08-05-1981                     | Gacek, M.                                       | All  |                |
|                          | 47.                   | EP 0 034 480 A2   | 08-26-1981                     | Gigg, et al.                                    | All  |                |
|                          | 48.                   | EP 0 091 761 B1   | 11-19-1987                     | Kawamatsu, et al.                               | All  |                |
|                          | 49.                   | EP 0 177 353 A2   | 09-04-1986                     | Meguro, et al.                                  | All  |                |
|                          | 50.                   | EP 0 186 405 A2   | 02-07-1986                     | Benedict, et al.                                | All  |                |
|                          | 51.                   | EP 0 230 068 A2   | 07-29-1987                     | Benedict, et al.                                | All  |                |
|                          | 52.                   | EP 0 243 173B1  | 06-26-1991                     | Oku, et al.                                     | All  |                |
|                          | 53.                   | EP 0 283 035 A1   | 09-21-1988                     | Iijima, et al.                                  | All  |                |
|                          | 54.                   | EP 0 354 322 A2   | 02-14-1990                     | DeVries, et al.                                 | All  |                |
|                          | 55.                   | EP 0 506 273 A2   | 09-30-1992                     | Arita, et al.                                   | All  |                |
|                          | 56.                   | EP 0 528 760 A1   | 02-24-1993                     | Hayakawa, et al.                                | All  |                |
|                          | 57.                   | EP 0 543 662 A2   | 05-26-1993                     | Fujita, et al.                                  | All  |                |
|                          | 58.                   | EP 0 559 079 A1   | 09-08-1993                     | Phan, et al.                                    | All  |                |
|                          | 59.                   | EP 0 603 419 A1   | 06-29-1994                     | Shibata, et al.                                 | All  |                |
|                          | 60.                   | EP 0 620 227 A1   | 10-19-1994                     | Yoshikawa, et al.                               | All  |                |
|                          | 61.                   | EP 0 636 630 A1   | 02-01-1995                     | Norcini, et al.                                 | All  |                |
|                          | 62.                   | EP 0 708 098 A1   | 04-24-1996                     | Yanagisawa, et al.                              | All  |                |
|                          | 63.                   | EP 0 745 600 A1   | 12-04-1996                     | Fujita, et al.                                  | All  |                |
|                          | 64.                   | EP 0 787 727 A1   | 08-06-1997                     | Nagao, et al.                                   | All  |                |
|                          | 65.                   | EP 0 861 666 A2   | 09-02-1998                     | Ikeda, et al.                                   | All  |                |
|                          | 66.                   | EP 0 489 663 A1   | 06-10-1992                     | Miyaoka, et al.                                 | All  |                |
|                          | 67.                   | EP 0 353 969 A1   | 02-07-1990                     | Wheland, et al.                                 | All  |                |
|                          | 68.                   | GB 1343022  | 01-09-1974                     | British Oxygen CO. LTD.                         | All  |                |

|                    |                 |
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| Sheet  | 3 | of | 10 | Attorney Docket Number   | MET-037CXT          |

|  |     |                                    |            |                       |     |  |
|--|-----|------------------------------------|------------|-----------------------|-----|--|
|  | 69. | GB 2271113 A                       | 04-06-1994 | Ichiro, et al.        | All |  |
|  | 70. | JP 07-002852 A2<br>(abstract only) | 01-06-1995 | Yoshioka, et al.      | All |  |
|  | 71. | JP 6-306089 A2<br>(abstract only)  | 01-11-1994 | Shoji, et al.         | All |  |
|  | 72. | JP 09-048770<br>(abstract only)    | 05-30-1996 | Sankyo, Co., Ltd.     | All |  |
|  | 73. | WO 90/09163                        | 08-23-1990 | Gensia Pharma         | All |  |
|  | 74. | WO 91/19721                        | 12-01-1991 | Glazier, A.           | All |  |
|  | 75. | WO 92/11269 A1                     | 07-09-1992 | Pohjala, et al.       | All |  |
|  | 76. | WO 92/12985 A1                     | 08-06-1992 | Thorn, et al.         | All |  |
|  | 77. | WO 92/19629 A1                     | 11-12-1992 | Mori, et al.          | All |  |
|  | 78. | WO 93/14081                        | 07-22-1993 | Adams, et al.         | All |  |
|  | 79. | WO 93/15610 A1                     | 08-19-1993 | Cox, et al.           | All |  |
|  | 80. | WO 94 07867                        | 04-14-1994 | Mylari, et al.        | All |  |
|  | 81. | WO 95/026347 A1                    | 10-05-1995 | Ohara, et al.         | All |  |
|  | 82. | WO 95/07920                        | 03-23-1995 | Bischofberger, et al. | All |  |
|  | 83. | WO 95/14385 A1                     | 06-01-1995 | Lindell, et al.       | All |  |
|  | 84. | WO 96/11196 A1                     | 04-18-1996 | Ohara, et al.         | All |  |
|  | 85. | WO 96/26207 A1                     | 08-29-1996 | Ohara, et al.         | All |  |
|  | 86. | WO 96/39401 A1                     | 12-12-1996 | Inman, et al.         | All |  |
|  | 87. | WO 97/10819                        | 03-27-1997 | Heyman, et al.        | All |  |
|  | 88. | WO 97/37688 A2                     | 10-16-1997 | Tamura, et al.        | All |  |
|  | 89. | WO 97/40051 A1                     | 10-30-1997 | Takatani, et al.      | All |  |
|  | 90. | WO 98/04528                        | 02-05-1998 | Schmidt, et al.       | All |  |

| NON PATENT LITERATURE DOCUMENTS |                       |  |                 |
|---------------------------------|-----------------------|--|-----------------|
| Examiner Initials*              | Cite No. <sup>1</sup> | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume issue number(s), publisher, city and/or country where published | T <sup>2</sup>  |
|                                 | 91.                   | Alimov, et al. "Preparation of amides on N-Phosphorylated amino carboxylic acids", Online, Chemical abstracts, Columbus, OH, April 25, 2003.   |                 |
|                                 | 92.                   | Amri, et al. "Regulation of adipose cell differentiation. I. Fatty acids are inducers of the aP2 gene expression", J. Lipid Res., pp. 1449-1456, 1991.   |                 |
| Examiner Signature              |                       |  | Date Considered |

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|  |      |   |  |
|--|------|---|--|
|  | 93.  | Arcoria, et al. "Reactions of Triethyl Phosphite with 2-Haloacetyl-furan, -thiophene, -pyrrole and -N-methylpyrrole (1)", J. Het. Chem., Vol. 12, pp. 215-218, 1975.  |  |
|  | 94.  | Ayral-Kaloustian, et al. "Synthesis of Partially-Protected D-fructofuranoses and D-fructose-6-phosphates" Carbohydrate Research, Vol. 214, pp. 187-192, Elsevier Science Publishers B.V., 1991.   |  |
|  | 95.  | Baudy, et al. "Potent Quinoxaline-Spaced Phosphono $\alpha$ -Amino Acids of the AP-6 Type as Competitive NMDA Antagonists: Synthesis and Biological Evaluation", J. Med. Chem., Vol. 36, No. 3, pp. 331-342, 1992.  |  |
|  | 96.  | Banker (Modern Pharmaceuticals) Banker, G.S. et al. "Modern Pharmaceuticals", 3 <sup>rd</sup> Edition, Marcel Dekker, New York, 1996, p. 451.   |  |
|  | 97.  | Benzaria, et al. "Synthesis in Vitro Antiviral Evaluation and Stability Studies of Bis(S-acyl-2-thioethyl) Ester Derivatives of 9-(2-(Phosphonomethoxy) ethyl)adenine (PMEA) as Potebtuak PMEA Prodrugs with Improved Oral Bioavailability", J. Med. Chem., Vol. 39, pp. 4958-4965, 1996. |  |
|  | 98.  | Brown, et al. "A novel N-aryl tyrosine activator of peroxisome proliferator-activated receptor- $\gamma$ reverses the diabetic phenotype of the Zucker diabetic fatty rat", Diabetes, Vol. 48, pp. 1415-1424, 1999.   |  |
|  | 99.  | Burke, et al. "Stereoselective Syntheses of the Rhizoxin C(1)-C(9) and C(12)-C(26) Subunits", Tetrahedron Letters, Vol. 39, pp. 2239-2242, 1998.  |  |
|  | 100. | Clark, et al. "Substituted dihydrobenzopyran and dihydrobenzofuran thiazolidine-2,4-diones as hypoglycemic agents", J. Med. Chem., Vol. 34, pp. 319-325, 1991.  |  |
|  | 101. | Corsano, et al. "A New Synthesis of Unsaturated Phosphonates (*) (**)", Gazzetta Chimica Italiana, Vol. 119, pp. 597-599, 1989.   |  |
|  | 102. | De Lombaert, et al. "N-Phosphonomethyl Dipeptides and Their Phosphonate Prodrugs, a New Generation of Neutral Endopeptidase (NEP, EC 3.4.24.11) Inhibitors", J. Med. Chem, pp. 498-511, 1994.   |  |
|  | 103. | Dizieree, et al. "A New Simple Method for the Synthesis of 1-Alkynylphosphonates using (EtO) <sub>2</sub> P(O)CCl <sub>3</sub> as Precursor", Tetrahedron Letters Vol. 37, No. 11, pp. 1783-1786, 1996.   |  |

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|  |      |  |  |
|--|------|--|--|
|  | 104. | Ebetino, et al. "A Stereoselective Process for the Preparation of Novel Phosphonoalkylphosphinates", Journal of Organometallic Chemistry, Vol. 529, pp. 135-142, 1997. |  |
|  | 105. | Farquhar, et al. "Biologically Reversible Phosphate-Protective Groups", Journal of Pharmaceutical Sciences, Vol. 72, pp. 324-325, 1983.                                |  |
|  | 106. | Foley, et al. "Rationale and Application of Fatty Acid Oxidation Inhibitors in Treatment of Diabetes Mellitus", Diabetes Care, Vol. 15, No. 6, pp. 773-784, 1992.      |  |
|  | 107. | Folli, et al. "Angiotensin II inhibits insulin signaling in aortic smooth muscle cells at multiple levels", J. Clin. Invest., Vol. 100, No. 9, pp. 2158-2169, 1997.    |  |
|  | 108. | Franchetti, et al. "Acyclic Nucleotides Related to Clitocine: Synthesis and Anti-HIV Activity", Nucleosides & Nucleotides, Vol. 14, No. 3-5, pp. 607-610, 1995.        |  |
|  | 109. | Freeman, et al. "Prodrug Design for Phosphates and Phosphonates", Progress in Medicinal Chemistry, p. 34, 1997.  |  |
|  | 110. | Fujita, et al. "Organic Synthesis Utilizing Thiazolidine and The Related Heterocycles", Heterocycles, Vol. 21, No. 1, pp. 41-60, 1984.                                 |  |
|  | 111. | Fujiwara, et al. "Characterization of new oral antidiabetic agent CS-045: Studies in KK and ob/ob mice and Zucker fatty rats", Diabetes, Vol. 37, pp. 1549-1558, 1988. |  |
|  | 112. | Garuti, et al. "Synthesis and Biological Evaluation of Some New Phosphates", Pharmazie, Vol. 47, pp. 295-297, 1992.  |  |
|  | 113. | Gastaldelli, et al. "Influence of Obesity and Type 2 Diabetes on Gluconeogenesis and Glucose Output in Humans", Diabetes, Vol. 49, pp. 1367-1373, 2000.                |  |
|  | 114. | Gerich, et al. "Matching Treatment to Pathophysiology in Type 2 Diabetes", Clinical Therapeutics, Vol. 23, No. 5, pp. 646-659, 2001.                                   |  |

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|  |   |    |    | First Named Inventor     | Paul D. van Poelje  |
|  |   |    |    | Art Unit                 | 1617                |
|  |   |    |    | Examiner Name            | Leonard M. Williams |
| Sheet  | 6 | of | 10 | Attorney Docket Number   | MET-037CXT          |

|  |      |  |  |
|--|------|--|--|
|  | 115. | Glucksman, et al. "Novel mutations and a mutational hotspot in the MODY3 gene", Diabetes, Vol. 46, pp. 1081-1086, 1997.  |  |
|  | 116. | Gohda, et al. "Theoretical Evidence of the Existence of a Diazafulvene Intermediate in the reaction Pathway of Imidazoleglycerol Phosphate Dehydratase: Design of Novel and Potent Heterocycle Structure for the Inhibitor on the Basis of the Electronic Structure-Activity Relationship Study", Biochimica et Biophysica Acta, Vol. 1385, pp. 107-114, 1998. |  |
|  | 117. | Grimaldi, et al. "Induction of a P2 gene expression by nonmetabolized long-chain fatty acids", Proc. Natl. Sci. USA, Vol. 89, pp. 10930-10934, 1992.   |  |
|  | 118. | Groop, "Sulfonylureas In NIDDM", Diabetes Care, Vol. 15, No. 6, pp. 737-754, 1992.   |  |
|  | 119. | Harada, et al. "Resolution of 1,3-Alkanediois via Chiral Spiroketal Derived from £Menthone" Tetrahedron Letters, Vol. 28, No. 41, pp. 4843-4846, 1987.   |  |
|  | 120. | Holst, et al. "Inhibition of the Activity of Dipeptidyl-Peptidase IV as a Treatment for Type 2 Diabetes", Diabetes, Vol. 47, pp. 1663-1670, 1998.  |  |
|  | 121. | Hoover, et al. "Indole-2-Carboxamide Inhibitor of Human Liver Glycogen Phosphorylase", J. Med. Chem., Vol. 41, pp. 2934-2938, 1998.  |  |
|  | 122. | Hulin, et al. "Novel thiazolidine-2,4-diones as potent euglycemic agents", J. Med. Chem., Vol. 35, pp. 1853-1864, 1992.  |  |
|  | 123. | Hundal, et al. "Mechanism by Which Metformin Reduces Glucose Production in Type 2 Diabetes", Diabetes, Vol. 49, pp. 2063-2069, 2000.   |  |
|  | 124. | Inzucchi, S.E. et al. "Efficacy and Metabolic Effects of Metformin and Troglitazone in Type II Diabetes Mellitus", N.E. Journal of Medicine, Vol. 338, No. 13, pp. 867-872, Massachusetts Medical Society, March 26, 1998.   |  |
|  | 125. | Khamnei, et al. "Neighboring Group Catalysis in the Design of Nucleotide Prodrugs", J. Med. Chem., Vol. 39, pp. 4109-4115, 1996.   |  |

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| Sheet  | 7 | of | 10 | Attorney Docket Number   | MET-037CXT          |

|  |      |  |  |
|--|------|--|--|
|  | 126. | Kolyamshin, et al. "Phosphorus-Containing Small Rings. VII* Amino Phosphorus Esters with a 2, 2-Dichlorocyclo-propyl Fragment", Russian Journal of Gen. Chem., Vol. 63, No. 1, pp. 29-33, 1993.  |  |
|  | 127. | Lehmann, et al. "An Antidiabetic thiazolidinedione is a high affinity ligand for peroxisome proliferator-activated receptor $\gamma$ (PPAR $\gamma$ )", J. Biol. Chem., Vol. 270, No. 22. pp. 12953-12956, 1995.                                       |  |
|  | 128. | Maier, et al. "Organic Phosphorus Compounds 97.1 Synthesis and Properties of 1-Amino-2-Aryl-and-2-Pyridyl-Ethylphosphonic Acids and Derivates", Phosphorus, Sulfur and Silicone, Vol. 62, pp. 15-27, 1991.   |  |
|  | 129. | Maruszezwska-Wieczorwska, et al. "Synthesis of 2-(Pyridyl)ethylphosphonic Acids and Esters", Chemical Abstracts, Vol. 23, pp. 1886-1889, 1958.   |  |
|  | 130. | Maruszezwska-Wieczorwska, et al. "Alkyl and Alkenyl Pyridines, Part VII. 3-(2'-Pyridyl)-Propylphosphonic Acid Alkilo I Alkenylopiyrdny, VII. Kwas 3-(2'-Pirydylo)-Propylofosfonowy", Roczniki ChemII Ann Soc. Chim. Polonorom, Vol. 37, p. 1315, 1963. |  |
|  | 131. | Mathisen, et al. "The effect of pioglitazone on glucose control and lipid profile in patients with type 2 diabetes", Diabetes, Vol. 48, Suppl. 1, 0441, 1998.  |  |
|  | 132. | Menard, et al. "Synthesis and Preliminary Evaluation of Chelating Resins Containing $\alpha$ -aminoalkylphosphonic Groups", Reactive Polymers, Vol. 32, pp. 201-212, 1994.   |  |
|  | 133. | Mikhailyuchenko, et al. "2-Chloro-1-(Diethoxyphosphinyl)Ethyl Isocyanate", Institute of Organic Chemistry, Vol. 47, No. 10, pp. 2011-2012, October 1977.   |  |
|  | 134. | Mikityuk, et al. "C-Acylation of Diazomethane with (Diethoxy-phosphinyl)Acetyl Chloride", UDC, Vol. 57, No. 7, pp. 1669-1670, July 1987.   |  |
|  | 135. | Mitchell, et al. "Bioreversible Protective for the Phospho Group: Bioactivation of the Di(4-acyloxybenzyl) and Mono(4-acyloxybenzyl) Phosphoesters of Methylphosphonate and Phosphonoacetate", J. Chem. Soc. Perkin Trans., pp. 2345-2353, 1992.       |  |
|  | 136. | Mori, et al. "Synthesis of Inhibitors of Imidazole Glycerol Phosphate Dehydratase", J. Am Chem Soc., Vol. 117, pp. 4411-4412, 1995.  |  |

|                       |  |                    |  |
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|   |   |    |    | Art Unit                 | 1617                |
|   |   |    |    | Examiner Name            | Leonard M. Williams |
| Sheet   | 8 | of | 10 | Attorney Docket Number   | MET-037CXT          |

|      |  |  |
|------|--|--|
| 137. | Morita, et al. "Synthesis and Antihypertensive Activities of 1, 4-Dihydropyridine-5-phosphonate Derivatives." Chem. Pharm Bull, Vol. 35, No. 9, pp. 3898-3904, 1987.   |  |
| 138. | O'Donnell, et al. "Preparation of an a-Aminophosphonate Cation Equivalent and its Reaction with organoboranes", Tetrahedron Letters, Vol. 35, pp. 6421-6424, 1994.   |  |
| 139. | Palacios, et al. "A "One Pot" Synthesis of Polysubstituted Pyridines from Metallated Alkylphosphonates, Nitriles and a, $\beta$ -Unsaturated Ketones", Tetrahedron Letters, Vol. 37, No. 26, pp. 4577-4580, 1996.          |  |
| 140. | Palacios, et al. "A New and Efficient Strategy for the Preparation of 1, 5, 2-Diazaphosphorines from Primary $\beta$ -Enaminophosphonates", Tetrahedron Lett., pp. 3091-3104, 1999.  |  |
| 141. | Palacios, et al. "A Simple and Efficient Strategy for the Preparation of 5-Phosphorylated Imidazol.-2-ones from Primary $\beta$ -Enaminophosphonates", Tetrahedron, Vol. 54, pp. 2281-2288, 1998.                          |  |
| 142. | Patel, et al. "Rosiglitazone monotherapy improves glycaemic control in patients with type 2 diabetes: A twelve-week, randomized, placebo-controlled study", Diabetes, Obesity and Metabolism, Vol. 1, pp. 165-172, 1999.   |  |
| 143. | Puech, et al. "Intracellular delivery of Nucleoside monophosphates through a reductase-mediated activation process", Antiviral Research Vol. 22, pp. 155-174, 1993.  |  |
| 144. | Reznick, et al. "Synthesis and Properties of Pyrimidinylalkylphosphonic Acids. 8. Interaction of Some Hydroxypyrimidines With Formaldehyde and Some Phosphorus (III) Derivatives", Organometallics, Vol. 83, p. 523, 1975. |  |
| 145. | Reznick, et al. "Synthesis and Properties of Pyrimidinylalkylphosphonic Acids., 6. Reaction of some Hydroxypyrimidines with Dibutyl 3-Chlorophosphonate", Chem Abs, Vol. 79, p. 380, 1973.                                 |  |
| 146. | Rizzi, et al. "PPN-type Nitrones: Preparation and use of a new series of $\beta$ -phosphorylated spin-trapping agents", J. Chem. Soc. Perkins Trans., Vol. 2, pp. 2513-2518, 1997.   |  |
| 147. | Saltiel, et al. "Thiazolidinediones in the treatment of insulin resistance and type II diabetes", Diabetes, Vol. 45, pp. 1661-1669, 1996.  |  |

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|  |      |  |  |
|--|------|--|--|
|  | 148. | Schmitz-Peiffer, et al. "Reversal of chronic alterations of skeletal muscle protein kinase C from fat-fed rats by BRL-49653", Am. J. Physiol., Vol. 273, pp. E915-E921, 1997.  |  |
|  | 149. | Serafinowska, et al. "Synthesis and in Vivo Evaluation of Prodrugs of 9-[2-(Phosphonomethoxy)ethoxy]adenine", J. Med. Chem., Vol. 38, pp. 1372-1379, 1995.   |  |
|  | 150. | Siddiqui, et al. "The Presence of Substituents on the Aryl Moiety of the Aryl Phosphoramidate Derivative of d4T Enhances Anti-HIV Efficacy in Cell Culture: A Structure--Activity Relationship", J. Med. Chem., Vol. 42, pp. 393-399, 1999.  |  |
|  | 151. | Smith, et al. "Synthesis and Biological Activity of Novel Cephalosporins Containing a (Z)-Vinyl Dimethylphosphonate Group", Vol. 48, No. 1, pp. 73-82, 1995.   |  |
|  | 152. | Starrett, et al. "Synthesis, oral bioavailability determination, and in vitro evaluation of prodrugs of the antiviral agent 9-[2-(phosphonomethoxy)ethyl]adenine (PNEA)", J. Med. Chem., Vol. 37, No. 12, pp. 1857-1864, 1994.   |  |
|  | 153. | Szczepaniak, et al. "Phosphoroorganic Complexones, Part VIII*. N-(Picolylamino)Isopropylphosphonic Acids", Polish J. of Chem., Vol. 52, pp. 721-726, 1978.   |  |
|  | 154. | Tontonoz, et al. "mPPARy2: Tissue specific regulator of an adipocyte enhancer", Gene and Development, Vol. 8, pp. 1224-1234, 1994.   |  |
|  | 155. | Tontonoz, et al. "Stimulation of Adipogenesis in fibroblasts by PPARy2, a lipid-activated transcription factor", Cell, Vol. 79, pp. 1147-1156, 1994.   |  |
|  | 156. | Valiquett, al et., "Troglitazone dose-response study in patients with NIDDM", Diabetes, Vol. 44, Suppl. 1, p. 406, 1995.   |  |
|  | 157. | Van Poelje, et al. "Combination Therapy with Pioglitazone and a Fructose 1, 6-Bisphosphatase Inhibitor (MB06322: CS-917) Improves Glycaemic Control and Lactate Homeostasis in Male Zucker Diabetic Fatty (ZDF) Rats" poster presented at the European Association for the Study of Diabetes (EASD), Copenhagen, Denmark, September 14-17, 2006. |  |

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|  | 158. | Willson, et al. "The Structure-activity relationship between peroxisome proliferator-activated receptor $\gamma$ agonism and the antihyperglycemic activity of thiazolidinediones", J. Med. Chem., Vol. 39, pp. 665-668, 1996. |  |
|  | 159. | Wolff, Manfred E. "Burger's Medicinal Chemistry and Drug Discovery", 5 <sup>th</sup> Edition, Vol. 1, John Wiley & Sons, 1995, pp. 975-977.  |  |
|  | 160. | Zask, et al. "Synthesis and antihyperglycemic activity of novel 5-(naphthalenylsulfonyl)-2, 4-thiazolidinediones", J. Med. Chem., Vol. 33, pp. 1418-1423, 1990.  |  |
|  | 161. | Zhao, et al. "Synthesis of Trans-4-Alkenyl Oxazoles", Tetrahedron Letters, Vol. 32, No. 13, pp. 1609-1612, 1991.   |  |
|  | 162. | "An Update on Type 2 Diabetes in Youth From the National Diabetes Education Program", Pediatrics, 2004, Vol. 114, pp. 259-263.   |  |

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